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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,431	07/30/2002	David M. Hockenberry	14538A-004610US	3708

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EXAMINER	
OWENS, AMELIA A	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 05/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,431	HOCKENBERRY ET AL.	
	Examiner	Art Unit	
	Amelia A. Owens	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15,20,21 and 23* is/are rejected.

7)☒ Claim(s) *14,16-19,22,24-26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-26 are pending. Drawings, 1 sheet, was filed with the application. Foreign priority was not claimed.

Information Disclosure Statement

The examiner considered the IDS.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13, 15,20-21, 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-13, 15 use the term 'agent' which is ambiguous. Is it functionally similar? Is it structurally close? How close is a structure of a material would be considered an agent? The metes and bounds of what would be within the scope of the claims being encompassed by the term 'agent' cannot be ascertained.

Claims 8,20-21, 23 use the term 'derivative' which is ambiguous since derivative is referring to material 'derived' from the named formula while applicants' material are the claimed formula. Therefore, it is recommended that all the terms 'derivative' be replaced with the term ---compound--- to be consistent with the named formula.

What is meant by the language 'binds to the hydrophobic pocket of the Bcl2 family member... formed by BH1, BH2.... Domains of the protein'? How is this determined?

For claim 11, it is noted that under the first chemical modification there is no definition for R1/R2/R3/R6, while under the second chemical modification there is no definition for R4/R5. What is meant exactly by the language 'first and second chemical modification'?

Claims 4 and 23 recites as species -- *(o) the compound of formula VII.* There is insufficient antecedent basis for this limitation in the claim. The formula is depicted at page 49 of the specification and the positions R1/R2 form a phenyl ring which is not provided for in the definition of claim 3/claim 21 respectively. Please check the claim for other such species.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,5,6,9-11, 13-15,17,20 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is an agent that modulates apoptosis by binding to a Bcl2 family member protein and preferentially induces apoptosis in a cell which over-expresses the Bcl2 family member protein; method for identifying an agent which modulates apoptosis of a cell; method of treating a subject having an apoptosis-associated disease. See claims 1, 11, 20 for example.

The state of the prior art and predictability: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. What is the scope of the term 'modulates apoptosis'? Modulation encompasses both inhibition and enhancement. Currently no single compound has been known to be able to function simultaneously both *inhibiting and enhancing* at the same time. Further, what is the scope of 'apoptosis-associated' disease? The specification does not reasonably provide enablement for the scope of the instant claim which encompasses using compounds of formula II to treat all possible apoptosis-associated diseases. Nor is it seen where the specification clearly sets forth what applicant means when using the term 'apoptosis-associated' disease.

Guidance and working examples: Several of the compounds have been prepared. It is noted that several tests were performed. However, the tests use antimycin A and other compounds specifically excluded by applicant. No correlation between the tests and the claimed utility of ---

modulating apoptosis; identifying agents which modulate apoptosis; or treating subject with apoptosis associated disease is noted. Nor have any of the claimed compounds been specifically shown to have the claimed utilities. Applicant is invited to come in with a declaration utilizing the clamed compound showing modulation of apoptosis; treating a subject with an apoptosis associated disease; and identifying an agent which modulates apoptosis.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for modulation of apoptosis; treating a subject with an apoptosis associated disease; and identifying an agent which modulates apoptosis. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound of claim 1 in order to practice the claimed invention.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims, with no assurance of success.

This rejection can be overcome by deleting the claims.

Claims 14,16-19,24-26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

Van Sickle USP 5,994,564 teach compounds similar to those of applicant. The difference is the positions of the dioxo groups; the positions R1/R2 form a phenyl; absence of

NH(CO)phenyl group. Compare column 2 lines 1-12 with instant claim 3. Therefore, the reference neither anticipates nor renders obvious the claimed compounds.

Ricks et al USP 6,335,660 B1 teach compounds similar to those of applicant. The difference is pyridyl instead of the instantly claimed phenyl bonded to the C(O)N. See abstract. Therefore, the reference neither anticipates nor renders obvious the claimed compounds.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amelia A. Owens whose telephone number is 571-272-0690. The examiner can normally be reached on Monday - Friday from 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amelia A. Owens
Primary Examiner
Art Unit 1625